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Research Article

Cardio-renal and Metabolic Comorbidity Clusters in High-Risk Diabetic Patients Selected for Ankle Block Anesthesia: A Retrospective Correlational Analysis

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Abstract

Patients with diabetic foot often have multiple cardio-renal and metabolic comorbidities, which increase perioperative risk, especially in resource-limited settings where ankle block anesthesia is commonly used. The aim of the present study was to identify clusters of these comorbidities in high-risk diabetic patients undergoing foot surgery with ankle block anesthesia and to study correlations among key clinical parameters relevant to perioperative risk. A retrospective correlational study was performed on 71 adult diabetic patients who underwent foot surgery with ankle block anesthesia at Diabetic General Hospital, Chattogram, Bangladesh. Demographic and clinical data, encompassing biochemical, haematologic, renal, and cardiac parameters, were obtained from hospital records. Spearman's rank correlation, principal component analysis (PCA), and hierarchical clustering were used to find patterns of multimorbidity. There were strong links between renal and metabolic variables. Serum creatinine (SC) exhibited a robust inverse correlation with estimated glomerular filtration rate (eGFR), whereas bicarbonate showed a negative correlation with creatinine, indicating a potential link between metabolic acidosis and renal dysfunction. Positive correlations between electrolytes, albumin, and hemoglobin signify homeostatic equilibrium. PCA identified two principal axes-metabolic-electrolyte integrity and renal dysfunction-that encompassed the majority of the variance. Hierarchical clustering delineated three distinct physiological groupings. These results emphasize the necessity for thorough preoperative assessment and multidisciplinary management to enhance perioperative outcomes in this high-risk population. Prospective studies are necessary to enhance risk assessment methodologies.

Keywords

Diabetic Foot, Cardio-renal Syndrome, Chronic Kidney Disease, Ankle Block Anesthesia, Perioperative Risk

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1. Introduction

Diabetes mellitus is one of the most common metabolic disorders in the world [1], and it is putting a lot of stress on healthcare systems in both rich and poor countries [2, 3]. In the last twenty years, the number of people with it has grown from 150 million in 2000 to 425 million in 2017. By 2045, it is expected to reach 629 million [2]. Bangladesh is one of the top eight nations in the world for diabetes, with over 13.1 million people affected, according to the International Diabetes Federation Atlas (10th edition, 2025) [4]. The socioeconomic impact is significant, with worldwide yearly costs for diabetes nearing US$760 billion and projected to increase to US$825 billion by 2030 [4]. The difficult course of treatment, expensive medical expenditures, and higher rates of complications put a lot of stress on patients' mental and financial health, making it a major public health problem [5].

Diabetic foot (DF) disease, especially diabetic foot ulcers (DFUs), is one of the most serious consequences of diabetes. Studies show that between 10 and 25% of people with diabetes will get a DFU at some point in their lives. About 5% of those people will have to have their limb amputated within five years of the ulcer starting [6]. These patients often have serious other health problems, such as heart disease, kidney problems, and neuropathy, which all increase the risk of surgery and make it harder to manage anesthesia [7]. For people who are at a high risk, regional anesthesia (RA) procedures, especially ankle block (AB), have become a useful alternative to general or neuraxial anesthesia, because neuraxial block needs fluid challenges, in ankles block which is not needed.

ABA has unique practical and physiological benefits, especially in settings with few resources [8]. By eliminating the necessity for extended fasting, it allows patients to sustain oral intake and persist with their standard diabetes medications, thereby facilitating perioperative glycaemic control-a vital element in wound healing and infection prevention [9]. The approach does not impede movement above the ankle, which makes it easier to move around after surgery, which could shorten the hospital stay and lower expenditures [10], even it can do as day care surgery. From an infrastructure point of view, AB is cheap and easy to get because it just needs basic equipment and local anesthetic. It doesn't need anesthesia machines or advanced monitoring. Because it is simple, it is especially useful for hospitals in distant areas or with few resources where specialized anesthetic services are hard to find [11].

Even with these practical advantages, the evidence foundation for selecting patients AB anesthetic. is still not well-developed [12]. Existing literature does not provide comprehensive characterization of the preoperative risk profiles and comorbidity patterns of DF patients considered appropriate for this method [13]. In particular, the intricate interconnections among comorbid conditions-such as ESRD (End stage renal disease), DCM (Dilated cardio myopathy), and nutritional deficiencies-are inadequately measured in this surgical cohort. A comprehensive correlational analysis of these comorbidity clusters is crucial to substantiate the clinical justification for the selection of AB, enhance perioperative risk stratification, and optimize care pathways in resource-limited (RL) environments.

Consequently, this study intends to fill this void by performing a retrospective, correlational analysis of patients with DF illness receiving AB anesthetic. in a RL environment. It aims to measure the preoperative comorbidity load, examine the interconnections among significant cardio renal and metabolic risk indicators, and delineate distinctive comorbidity clusters within this high-risk (HR) cohort. The results will yield an evidence-based profile of patients chosen for this anesthetic method and enhance safer, more effective perioperative treatment in resource-constrained settings.

2. Methods and Materials

2.1. Study Design and Setting

This retrospective study was conducted at Diabetic General Hospital, Khulshi, Chattogram, Bangladesh, a tertiary referral center specializing in the management of diabetes and its complications [14]. The hospital serves both urban and rural populations and manages a high volume of patients with advanced DF disease requiring surgical intervention [15]. Multidisciplinary services include endocrinology, orthopedic surgery, anesthesia, wound care, and laboratory support [16]. In this RL setting, RA-particularly AB -is routinely employed for distal foot procedures in HR patients with significant cardio-renal-metabolic comorbidities [17, 18]. The institution maintains structured clinical records, facilitating retrospective observational research [19]. Medical records of eligible patients were reviewed over a six-month data abstraction period. The study included patients admitted within a six months' time-frame who underwent foot surgery under ABA. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [20].

2.2. Study Population and Eligibility Criteria

This retrospective observational study included 71 adult diabetic patients recruited from the Department of Orthopedics at Diabetic General Hospital, Khulshi, Chattogram, Bangladesh, between June 15 and December 25, 2025. All eligible participants underwent DF surgery performed under ABA. Inclusion criteria comprised patients aged 35-87 years with a confirmed diagnosis of diabetes mellitus who required surgical intervention for diabetic foot–related complications. Preoperative assessments were conducted jointly by orthopedic consultants and anesthesiology teams following standardized

institutional protocols to evaluate surgical eligibility, anesthetic suitability, and perioperative risk status. Demographic characteristics, clinical variables, and comorbidity profiles were extracted retrospectively from hospital medical records for subsequent analysis. All surgical procedures were performed using ABA. Patients were excluded if they had major amputation distal to the ankle or above the ankle, wounds located above the ankle joint, incomplete clinical or laboratory documentation, or severe psychiatric illness.

2.3. Data Collection and Variables

Data were collected retrospectively using a structured case record review form. Demographic variables recorded included age and sex. Relevant clinical parameters encompassed duration of diabetes, type of DF lesion, type of surgical procedure, and duration of surgery. Cardio-renal comorbidities such as hypertension, ischemic heart disease, chronic kidney disease, and heart failure (if documented) were noted. Metabolic comorbidities included electrolyte imbalance, abnormal lipid profile, glycemic control measures (HbA1c or fasting blood glucose, where available), and obesity based on body mass index when recorded. Comorbidities were determined from physician documentation or ongoing treatment, and each condition was coded as a binary variable indicating its presence or absence.

2.4. Anesthetic Technique and Intraoperative Assessment

All patients received ABA using a landmark-guided anatomical technique, with 2-3 mL of 2% bupivacaine diluted with normal saline to achieve a total volume of 6 mL. Block adequacy was clinically assessed prior to incision and categorized as complete, in which surgery was completed without supplemental anesthesia, or partial, requiring additional anesthesia. Intraoperative hemodynamic stability and any adverse events were documented from the anesthetic charts [21].

2.5. Surgical Procedures

The surgical interventions performed included toe amputation, trans metatarsal amputation, localized debridement, and abscess drainage. The operative procedures ranged in duration from 30 to 60 minutes, and none required conversion to general anesthesia.

2.6. Outcome Measures

The primary outcome of this study was the identification and description of cardio-renal-metabolic multimorbidity patterns among HR patients undergoing DF surgery. Secondary outcomes included the distribution of an AB success (complete versus partial), the association between multimorbidity burden and anesthetic outcome, and the perioperative safety profile. It can also do in low resource support.

2.7. Statistical Analysis

Statistical analyses were conducted using Origin 2024, R, and Excel. Normality was evaluated using the Shapiro–Wilk test and Q-Q plots [22]. Variables with normal distributions were reported as mean ± standard deviation, while non-normally distributed variables were presented as median and interquartile range. As only five variables exhibited normality, Spearman's rank correlation coefficient was applied for pairwise comparisons to address deviations from normality. This nonparametric method is suitable for assessing monotonic relationships, which are pertinent to biological data. Correlation coefficients were classified from very weak to very strong. Multimorbidity patterns were analyzed using frequency distributions and hierarchical clustering with Ward's method. Associations with anesthetic outcomes were examined using appropriate statistical tests, including logistic regression to evaluate the relationship between comorbidities and partial block occurrence. Statistical significance was set at $p < 0.05$.

2.8. Sample Size Consideration

As a retrospective study, all eligible cases within the defined study period (n = 71) were included. The sample size was deemed sufficient for descriptive and exploratory analyses, though it may limit statistical power for multivariable modeling.

3. Result and Discussion

The present study investigated a cohort of 71 participants recruited from the Department of Orthopedics at Diabetic General Hospital, Khulshi, Chattogram, Bangladesh, between June 15 to December 25, 2025. The study population comprised 38 males (53.5%) and 33 females (46.5%) participants (Figure 1b), with a mean age of 53.8 ±9.3 years (range: 27 to 73 years). All participants underwent comprehensive clinical and laboratory evaluation, including assessment of hematological parameters (hemoglobin), biochemical markers (serum electrolytes, including sodium, potassium, and chloride; renal function (RF) markers, including SC and eGFR; nutritional indicators, including serum albumin (SA), and acid-base status (bicarbonate levels).

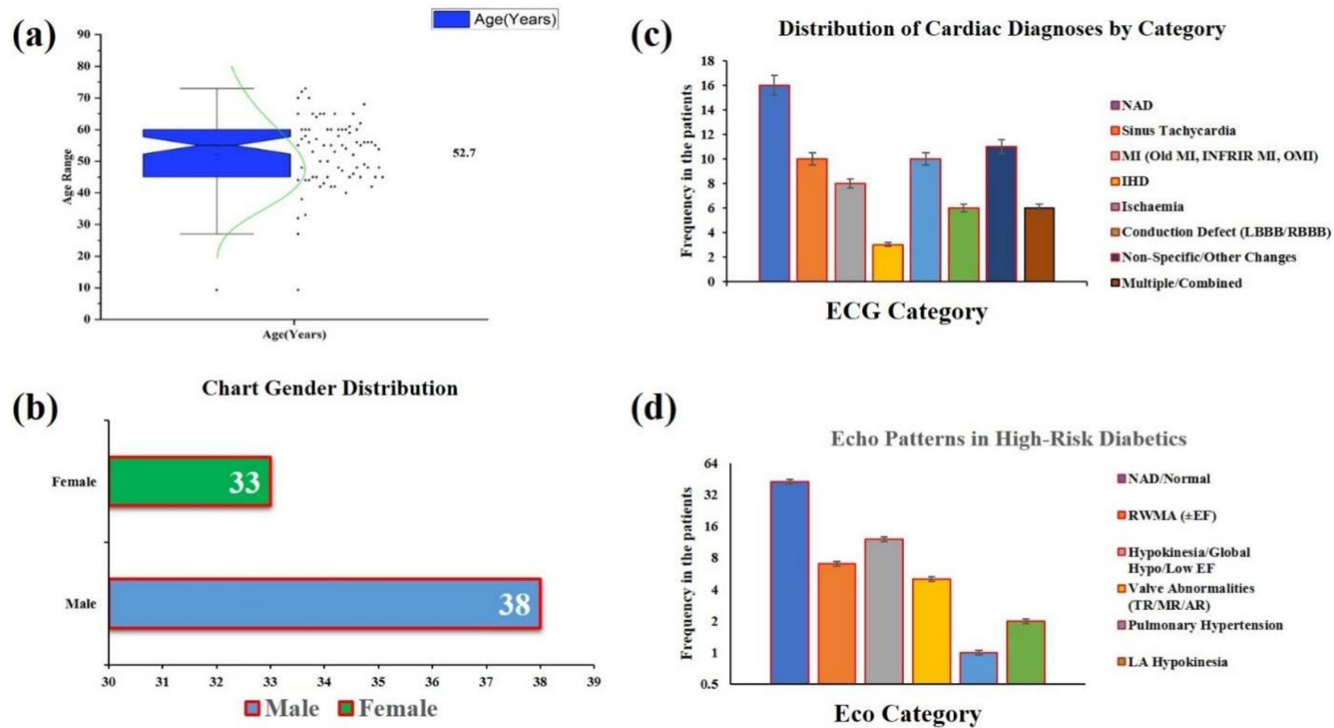

Figure 1. *Clinical characteristics of the study population: (a) Age distribution with box-plot and density curve; (b) Gender distribution; (c) Distribution of electrocardiographic diagnostic categories; and (d) Echocardiographic patterns among high-risk diabetic patients.*

Additionally, all participants underwent electrocardiographic (ECG) and echocardiographic evaluation to assess cardiac status. The mean hemoglobin level was 10.5 ± 1.7 g/dL, the mean SA was 3.2 ±0.9 g/dL, and the mean electrolyte levels were as follows: sodium 133.5 ±4.5 mEq/L, potassium 4.2 ±0.6 mEq/L, chloride 100.0 ±7.2 mEq/L, and bicarbonate 23.5 ±2.8 mEq/L. The mean SC was 1.7 ±1.7 mg/dL, with a corresponding mean eGFR of 62.8 ±21.9 mL/min/m², indicating a spectrum of RF from normal to moderately impaired. ECG analysis revealed diverse cardiac findings, with the majority of participants showing non-specific changes (n=11), followed by sinus tachycardia (n=10), ischemic changes (n=10), normal traces (NAD, n=16), myocardial infarction patterns (n=8), conduction defects (n=6), and multiple combined abnormalities (n=6) (Figure 1c). Echocardiographic evaluation demonstrated that the majority of participants had normal findings (NAD/Normal, n=43), while others exhibited various abnormalities, including hypokinesia or global hypokinesia with reduced ejection fraction (n=12), regional wall motion abnormalities (n=7), valve abnormalities (n=5), pulmonary hypertension (n=1), and left atrial hypokinesia (n=2) (Figure 1d). This comprehensive dataset enabled a detailed investigation of the interrelationships among demographic factors, hematological parameters, electrolyte balance (EB), RF, and cardiac status in this study population. Cardio-Renal (CR) and Metabolic Interrelationships: Spearman Correlation Analysis.

A Spearman rank correlation analysis was conducted to examine the interrelationships among cardiovascular and renal, as well as metabolic, parameters in HR diabetic patients selected for ABA.

3.1. Renal Function and Metabolic Acidosis

Spearman's rank correlation analysis revealed a strong inverse relationship between SC and eGFR (ρ = -0.701, $p < 0.001$), confirming a wide spectrum of chronic kidney disease (CKD) severity within the cohort. Critically, a moderate, highly significant inverse correlation was identified between SC and bicarbonate levels (ρ = -0.390, $p < 0.001$), while a corresponding moderate positive correlation was observed between eGFR and bicarbonate (ρ = 0.409, $p < 0.001$). These findings demonstrate that declining RF is strongly and significantly associated with the development of metabolic acidosis (MA) in this population (Table 1).

Declining RF in this cohort was strongly demonstrated by the inverse correlation between SC and eGFR, while the significant inverse association between creatinine and bicarbonate and the positive correlation between glomerular filtration rate and bicarbonate indicate that worsening renal dysfunction was accompanied by MA. These findings are consistent with Caravaca et al. 1999 [23] who described MA as a near-invariable consequence of advanced renal failure, although diabetic patients in their cohort showed comparatively less severe bicarbonate reduction. Similar studies documented that impaired renal acid excretion in CKD contributes directly to bicarbonate decline [24-26]. More recently, Machado et al. 2023 [27] demonstrated that dietary acid load independently

increased CKD risk in type 2 diabetes, while perioperative evidence from Kraut and Madias 2015 [28] highlighted increased metabolic vulnerability in diabetic surgical patients. Our findings extend these observations to a low-resource, perioperative diabetic population, emphasizing routine metabolic assessment to reduce risk.

3.2. Electrolyte Disturbances

Significant inter-correlations were observed among serum electrolytes. Potassium demonstrated a moderate positive correlation with albumin (ρ = 0.338, p = 0.004) and with chloride (ρ = 0.334, p = 0.004). Chloride also exhibited a moderate positive correlation with hemoglobin (ρ = 0.312, p = 0.008) and with sodium (ρ = 0.305, p = 0.009). Additionally, a weak-to-moderate positive correlation was noted between sodium and potassium (ρ = 0.272, p = 0.020). Although potassium demonstrated a negative correlation with bicarbonate in the expected direction (ρ = -0.201), this association did not reach statistical significance (p = 0.089) (Table 1).

The present study demonstrated significant interrelationships among serum electrolytes, indicating coordinated metabolic regulation in HR diabetic patients undergoing ABA. The positive correlation between potassium and chloride suggests a link in renal tubular handling of major intracellular and extracellular ions, particularly in diabetic patients, where subtle renal dysfunction may alter electrolyte homeostasis. The positive association between sodium and potassium also reflects preserved but vulnerable EB, consistent with reports that diabetic patients often exhibit parallel sodium–potassium shifts due to insulin resistance, altered cellular transport, and renal compensation. The moderate positive correlation between potassium and SA may indicate that better nutritional status supports intracellular electrolyte stability, as hypoalbuminemia is frequently associated with metabolic stress and electrolyte imbalance. Similarly, the correlations of chloride with hemoglobin and sodium suggest that chloride may reflect both hydration status and acid–base adaptation. Comparable observations have been reported by Korus et al. 2025 [29], who emphasized that chloride is an important determinant of metabolic compensation in chronic kidney disease. Although potassium showed an inverse relationship with bicarbonate, the lack of statistical significance suggests that an overt potassium-driven acid–base disturbance was limited in this cohort, possibly due to compensatory renal and perioperative metabolic mechanisms.

3.3. Age-Related Associations

Age was significantly correlated with several clinical parameters. A moderate positive correlation was identified between age and serum sodium (ρ = 0.315, p = 0.007), while a weak negative correlation was observed between age and eGFR (ρ = -0.236, p = 0.044), reflecting the anticipated age-related decline in kidney function. Age showed a positive trend with serum potassium (ρ = 0.209, p = 0.075) (Table 1), but this did not reach statistical significance.

Our study demonstrated significant age-related biochemical variation among HR diabetic patients, with age showing a moderate positive correlation with serum sodium and a weak inverse correlation with eGFR. The decline in glomerular filtration rate with advancing age is consistent with established physiological evidence that renal filtration capacity gradually decreases because of nephron loss, reduced renal perfusion, and progressive vascular sclerosis, effects that are often accelerated in diabetic individuals. Similar findings have been reported by Koch and Fulop 2017 [30], who identified age as an independent determinant of reduced RF in CKD populations. The positive association between age and sodium may reflect reduced renal concentrating ability, altered water balance, and age-related endocrine changes affecting sodium regulation [31]. A similar age-associated rise in sodium has been described in diabetic and elderly metabolic cohorts [32]. Although potassium showed only a non-significant positive trend, this may indicate early age-related impairment of potassium handling, which remains partially compensated under stable perioperative conditions.

3.4. Nutritional and Hematological Parameters

SA and hemoglobin, markers of nutritional status and anemia, respectively, demonstrated trends consistent with the pathophysiology of chronic kidney disease. Albumin showed a weak inverse correlation with SC (ρ = -0.172, p = 0.146) and a weak positive correlation with bicarbonate (ρ = 0.138, p = 0.244), though neither reached statistical significance. Similarly, hemoglobin demonstrated a weak inverse correlation with SC (ρ = -0.137, p = 0.249) and a weak positive correlation with eGFR (ρ = 0.188, p = 0.112) (Table 1), suggesting trends toward anemia of CKD that did not achieve statistical significance in this cohort.

In this cohort, SA and hemoglobin demonstrated weak, non-significant correlations with RF markers, trends that align directionally with the established pathophysiology of the cardio-renal-anemia syndrome. The observed weak inverse association between SA and creatinine and the positive trend with bicarbonate suggest early nutritional and metabolic alterations accompanying renal dysfunction in diabetic patients, although statistical significance was not achieved. Similar findings have been reported in diabetic CKD populations, where declining albumin reflects protein loss, chronic inflammation, and reduced nutritional reserve [33, 34]. Previous studies have shown that hypoalbuminemia is frequently associated with worsening renal outcomes and increased cardiovascular vulnerability in diabetic patients. Hemoglobin also demonstrated expected directional trends, with lower values accompanying higher creatinine and relatively preserved levels with better GFR, consistent with early anemia of CKD caused by reduced erythropoiesis and chronic inflammation [35]. Comparable studies in type 2 diabetes have reported gradual hemoglobin decline even in moderate renal dysfunction. The absence of statistical significance may be explained by limited sample

size (n=71), heterogeneous renal status (early-stage CKD, mean GFR 62.8 mL/min/m^2), range restriction due to anesthesia selection, and overlapping cardio metabolic comorbidities, factors well recognized to attenuate correlation strength in low-resource settings.

Table 1. *Spearman correlation matrix illustrating the interrelationships among cardio-renal and metabolic parameters in high-risk diabetic patients (n = 70-71). Correlation coefficients (ρ) are displayed, with values closer to ±1 indicating stronger associations.*

		Age (Years)	Hb%	Albumin Level	Na+	K+	Cl-	HCO3	Serum Creatinine	GFR
Age (Years)	Spearman Corr.	1	0.07297	-0.02863	0.31516	0.20939	0.19574	-0.09797	0.16848	-0.23618
	p-value	--	0.53954	0.80996	0.00661	0.07542	0.09939	0.40961	0.15419	0.04426
Hb%	Spearman Corr.	0.07297	1	0.12139	0.21767	0.03685	0.31182	0.06046	-0.13672	0.18751
	p-value	0.53954	--	0.30628	0.06432	0.75693	0.00767	0.61137	0.24875	0.11217
Albumin Level	Spearman Corr.	-0.02863	0.12139	1	0.1703	0.33751	0.03016	0.13798	-0.17192	0.1023
	p-value	0.80996	0.30628	--	0.14973	0.0035	0.80144	0.24438	0.14585	0.38913
Na+	Spearman Corr.	0.31516	0.21767	0.1703	1	0.2719	0.30463	-0.17715	0.02277	-0.00193
	p-value	0.00661	0.06432	0.14973	--	0.01996	0.00927	0.13379	0.84837	0.98704
K+	Spearman Corr.	0.20939	0.03685	0.33751	0.2719	1	0.33404	-0.20051	0.11415	0.01169
	p-value	0.07542	0.75693	0.0035	0.01996	--	0.00413	0.08897	0.33624	0.92183
Cl-	Spearman Corr.	0.19574	0.31182	0.03016	0.30463	0.33404	1	-0.19869	0.17667	-0.02442
	p-value	0.09939	0.00767	0.80144	0.00927	0.00413	--	0.09429	0.13767	0.83866
HCO3	Spearman Corr.	-0.09797	0.06046	0.13798	-0.17715	-0.20051	-0.19869	1	-0.39045	0.40931
	p-value	0.40961	0.61137	0.24438	0.13379	0.08897	0.09429	--	6.37658E-4	3.23599E-4
Serum Creatinine	Spearman Corr.	0.16848	-0.13672	-0.17192	0.02277	0.11415	0.17667	-0.39045	1	-0.70066
	p-value	0.15419	0.24875	0.14585	0.84837	0.33624	0.13767	6.37658E-4	--	<0.0001
GFR	Spearman Corr.	-0.23618	0.18751	0.1023	-0.00193	0.01169	-0.02442	0.40931	-0.70066	1
	p-value	0.04426	0.11217	0.38913	0.98704	0.92183	0.83866	3.23599E-4	<0.0001	--

2-tailed test of significance is used

In summary, the most robust and statistically significant finding in this analysis is the strong association between renal impairment and MA, as evidenced by the highly significant correlations between creatinine, eGFR, and bicarbonate (all $p < 0.001$). Significant intercorrelations among electrolytes (sodium, potassium, chloride) further characterize the complex electrolyte disturbances in this HR diabetic and hypertensive population. Age-related decline in kidney function was confirmed, while nutritional and hematological parameters demonstrated expected directional trends that did not reach statistical significance, potentially due to sample size limitations or confounding comorbidities.

3.5. Acid-Base Patterns

Bicarbonate demonstrated consistent negative correlations with both chloride (ρ = -0.247) and potassium (ρ = -0.247) (Table 1). These inverse relationships are clinically consistent with patterns observed in metabolic acid-base disorders, specifically non-anion gap hyperchmoremic acidosis both common complications in diabetic kidney disease.

This correlational analysis identifies distinct CR and metabolic comorbidity clusters in HR diabetic patients undergoing ABA. The significant associations-particularly the creatinine-bicarbonate axis, the potassium-albumin nutritional link, and the electrolyte interdependence patterns-highlight the complex physiological interactions that must be considered in perioperative risk stratification and management.

The inverse correlations between bicarbonate and chloride, and between bicarbonate and potassium, observed in this study are consistent with established acid–base disturbances in diabetic kidney disease, in which reduced bicarbonate is

commonly accompanied by hyperchloremic MA and potassium retention. Similar findings have been reported in CKD cohorts, in which declining bicarbonate reflects impaired renal acid excretion and compensatory chloride retention, leading to non-anion gap MA [36-38]. Previous studies also described an inverse relationship between bicarbonate and potassium, as MA promotes an extracellular potassium shift and reduced renal potassium clearance [39, 40]. Although the correlations in this cohort were modest, they support early metabolic instability frequently documented in diabetic patients with evolving renal dysfunction.

3.6. Principal Component Analysis (PCA)

Principal component analysis with varimax rotation was conducted to identify underlying comorbidity clusters among the nine clinical variables. Sampling adequacy was confirmed (KMO = 0.68), and Bartlett's test of sphericity was significant ($p < 0.001$), supporting the suitability of the data for dimension reduction. Two components with eigenvalues greater than 1 were extracted, collectively explaining 60.8% of the total variance. Component 1 (PC1) explained 40.8% of the variance (Figure 2) and demonstrated high positive loadings from sodium (0.475), chloride (0.454), potassium (0.367), bicarbonate (0.360), hemoglobin (0.354), age (0.299), and albumin (0.236). This component was interpreted as a 'Metabolic-Electrolyte Integrity' axis, reflecting overall metabolic and electrolyte homeostasis.

Component 2 (PC2) explained 20.0% of the variance (Figure 2) and was characterized by a strong positive loading from SC (0.626) and strong negative loadings from estimated GFR (-0.614) and bicarbonate (-0.301), with a moderate contribution from age (0.305). This component was interpreted as a 'CR' axis, capturing the spectrum of renal impairment and its associated acid-base disturbance. The loading plot visually confirmed the separation of these clusters, with metabolic-electrolyte variables clustering along PC1 and RF markers distributed along PC2. These findings demonstrate that CR and metabolic disturbances represent distinct but interrelated comorbidity dimensions in this HR diabetic surgical population.

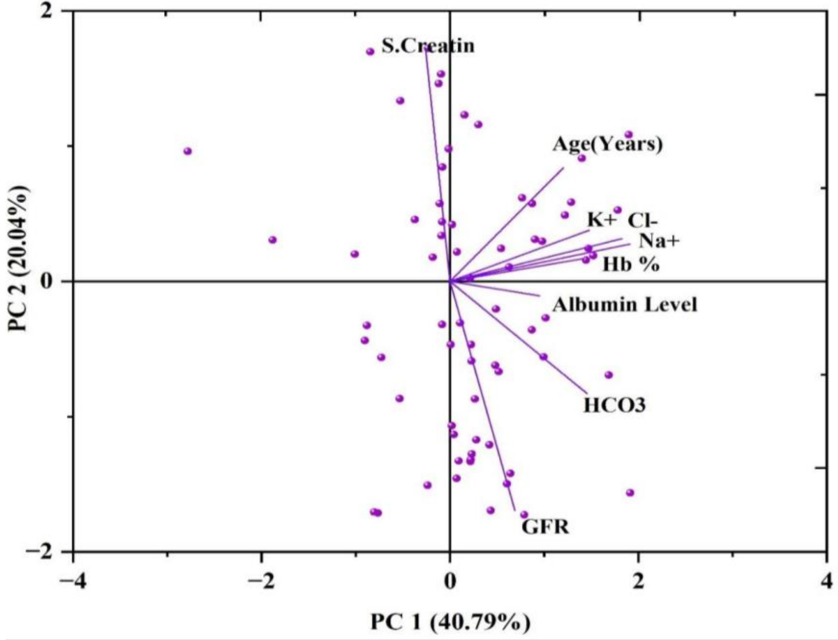

Figure 2. Principal component analysis revealing two distinct comorbidity clusters. Cluster 1 (PC1, 40.79%): Metabolic-electrolyte variables including Na^+, Cl^-, K^+, HCO_3^-, Hb%, albumin, and age. Cluster 2 (PC2, 20.04%): Renal function markers with creatinine opposing GFR and bicarbonate. Together, these components explain 60.83% of the total variance in the dataset.

The PCA identified two clinically meaningful comorbidity dimensions, consistent with previous studies that have described clustered metabolic and renal abnormalities in diabetic populations [41, 42]. PC1, dominated by sodium, chloride, potassium, bicarbonate, hemoglobin, albumin, and age, reflects a metabolic–electrolyte integrity axis similar to earlier analyses of diabetic cohorts, in which EB and nutritional markers clustered as indicators of systemic metabolic stability (Chen et al., 2024) [43]. PC2, driven by positive creatinine and negative GFR and bicarbonate loadings, corresponds to the classical CR axis reported in CKD studies, in which declining filtration capacity closely associates with acid–base disturbances [28, 44]. Comparable multivariate studies have shown that renal dysfunction and metabolic derangements emerge as distinct but interconnected components in HR diabetic patients [42, 45].

3.7. Hierarchical Cluster Analysis

Hierarchical cluster analysis using the group average method with correlation distance was performed to identify natural groupings among the nine clinical variables. The analysis revealed three distinct comorbidity clusters (Figure 3).

Cluster formation followed a stepwise hierarchy. Bicarbonate and GFR clustered first at the smallest distance (0.544), confirming the physiological link between kidney function and acid-base balance. Hemoglobin and chloride formed a metabolic-hydration pair (distance 0.726), while sodium and potassium formed the electrolyte core (distance 0.727). Albumin subsequently joined the sodium-potassium cluster (distance 0.785), establishing nutritional-electrolyte integration. Age and SC clustered at a distance of 0.853, forming an age-renal axis that later merged with the expanding metabolic cluster. The renal acid-base cluster (bicarbonate and GFR) integrated last at the greatest distance (1.135), confirming its distinct yet related nature.

Similarity analysis quantified the strength of relationships within clusters. The strongest relationship was observed between age and SC (similarity 75.09), indicating that renal impairment is strongly age-dependent. A strong link was also found between albumin and potassium (similarity 69.17), reflecting shared nutritional and metabolic variance. Expected electrolyte interdependence was confirmed between sodium and potassium (similarity 64.00), while hemoglobin and chloride showed moderate similarity (63.90), suggesting shared variance related to hydration status. Bicarbonate and GFR demonstrated moderate similarity (47.94), consistent with their physiological connection.

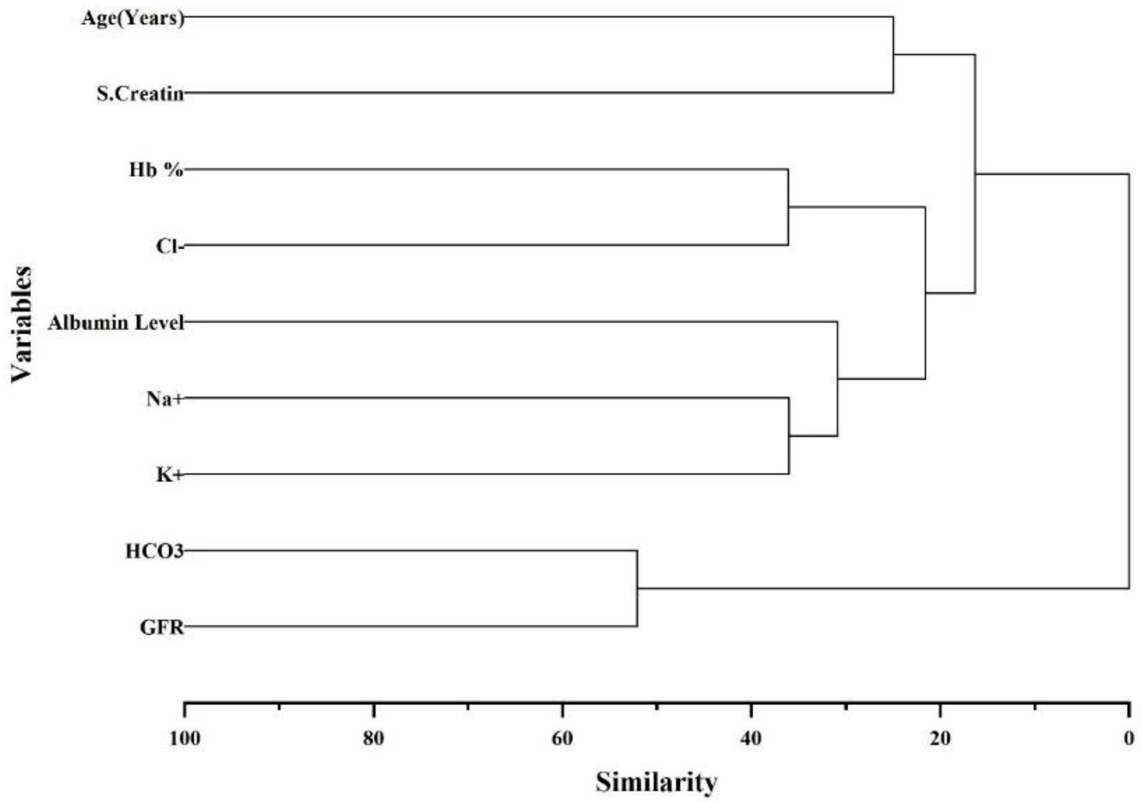

Figure 3. Multidimensional Comorbidity Clusters in Diabetic Patients: A Cardio-Renal-Metabolic Perspective.

Three distinct clusters emerged from the analysis:

Cluster 1 (Age-Renal Axis) comprised age and SC, representing the strong age-dependent progression of renal impairment in this diabetic cohort. Cluster 2 (Metabolic-Electrolyte-Nutrition) encompassed hemoglobin, chloride, sodium, potassium, and albumin, capturing global metabolic health, including oxygen-carrying capacity, hydration status, EB, and nutritional status. The strong albumin-potassium link suggests nutritional status and intracellular electrolyte homeostasis are physiologically intertwined.

Cluster 3 (Renal-Acid Base Axis) consisted of bicarbonate and GFR, confirming the fundamental connection between kidney function and acid-base homeostasis. Its late integration with the main hierarchy indicates this axis represents a distinct physiological dimension. In summary, hierarchical cluster analysis identified three distinct but interrelated comorbidity clusters-an Age-Renal Axis, a Metabolic-Electrolyte-Nutrition Cluster, and a Renal-Acid Base Axis-providing a framework for understanding physiological parameter aggregation in this HR diabetic surgical population.

Hierarchical cluster analysis revealed three distinct comorbidity clusters in this HR diabetic cohort, consistent with previous multivariate studies in diabetic populations [42]. The early clustering of bicarbonate and GFR (distance 0.544) confirms the well-established physiological link between RF and acid-base homeostasis, as described in CKD literature [28]. The metabolic-electrolyte-nutrition cluster (hemoglobin, chloride, sodium, potassium, albumin) mirrors findings from large diabetic cohort analyses, in which nutritional and electrolyte markers aggregate as indicators of systemic metabolic stability [43]. The strong similarity between age and SC (75.09%) aligns with longitudinal studies demonstrating age-dependent progression of diabetic nephropathy [46]. Notably, the renal-acid base axis integrated last (distance 1.135), suggesting it represents a distinct physiological dimension rather than a secondary manifestation of metabolic derangement-a finding supported by recent cluster analyses in diabetic kidney disease [45].

4. Conclusions

This study shows that specific combinations of heart, kidney, and metabolic conditions affect the surgical risk for HR diabetic patients who receive ABA in settings with limited resources. Our analyses found strong links between kidney problems and MA, as well as complex relationships involving metabolism, electrolytes, and age-related kidney changes. These patterns suggest that careful preoperative assessment is important and support the use of ankle block safely anesthesia for these patients. Our findings highlight the urgent need for risk-stratification tools based on these clusters and for further studies across multiple centers to improve outcomes for people undergoing DF surgery.

Limitation of study

A notable limitation of this study is that many patients do not fully understand how a minimal dose of anesthesia can effectively facilitate amputation procedures. Consequently, extra time must be allocated to patient education and reassurance, which can inadvertently delay the overall treatment process and affect clinical workflow. Additionally, patients' fear and apprehension regarding the procedure may heighten anxiety levels, potentially leading to further complications or negatively influencing the success of the intervention. These factors underscore the importance of addressing both informational and psychological barriers to optimize patient outcomes.

Ethics committee approval

This study is a retrospective analysis of anonymized data from existing hospital records, with no direct patient involvement or intervention. Participation was entirely voluntary, and the study was carried out with the aim of improving medical practice and societal welfare. In accordance with institutional policy and national regulations, and given the nature of the study, approval from the institutional ethics committee was not required.

Human Ethics and Consent to Participate declarations

No experiments were done on humans or animals for this study. This research was a retrospective examination of the medical records of patients who had already received conventional clinical care at Diabetic General Hospital, Chattogram, Bangladesh. All procedures performed were in compliance with the institutional norms and in accordance with the ethical standards of the Declaration of Helsinki and the relevant legislation of the clinical research ethics committee. For the purpose of this study, no other interventions or variations from usual patient care were made. Data collection and analysis were conducted in accordance with patient confidentiality.

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent

We declare that no identifiable patient data appear in this article. As per institutional guidelines for retrospective studies using de-identified data, individual informed consent was not required. The authors affirm that all data were handled with strict attention to privacy and confidentiality.

Abbreviations

PCA	Principal Component Analysis
SC	Serum Creatinine
eGFR	Estimated Glomerular Filtration Rate
DF	Diabetic Foot
DFU	Diabetic Foot Ulcers
RA	Regional Anesthesia
AB	Ankle Block
ESRD	End Stage Renal Disease
DCM	Dilated Cardio Myopathy
RL	Resource-limited
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
RF	Renal Function
SA	Serum Albumin
CR	Cardio-Renal
EB	Electrolyte Balance
MA	Metabolic Acidosis
CKD	Chronic Kidney Disease
HR	High Risk

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Author Contributions

Tasnuva Tanzil: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft

Md. Mazharul Islam: Conceptualization, Formal analysis, Visualization, Supervision, Writing – review & editing

Md. Mostafa Al Bani: Investigation, Methodology, Validation

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Data Availability Statement

The datasets generated and/or analysed during the current study are not publicly available due to subject confidentiality, but they are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors confirm that they have no financial interests or personal relationships that could have influenced the work presented in this paper.

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